Systematic review: blood pressure target in chronic kidney disease and proteinuria as an effect modifier

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**CRD summary**
This review did not find evidence that treatment to achieve a lower blood pressure target improved outcomes compared with a higher target in adults with chronic kidney disease. Benefits were also uncertain for the subgroup of patients with proteinuria. Despite some limitations in the review methods and reporting, the authors’ conclusions seem likely to be reliable.

**Authors’ objectives**
To compare the effects of lower versus higher blood pressure targets in adults with chronic kidney disease and different levels of proteinuria.

**Searching**
MEDLINE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from July 2001 to January 2011. Additional articles were identified from a systematic search conducted in 2004, which included articles indexed in MEDLINE from 1966 to 2002. There were no language restrictions.

**Study selection**
Randomised controlled trials (RCTs) and observational follow-up reports of RCTs that compared blood pressure targets in adults with non dialysis-dependent chronic kidney disease were eligible. Studies had to report at least one of the outcomes of mortality, kidney failure, clinical cardiovascular events, categorical change in kidney function, rate of change in glomerular filtration rate, number of antihypertensive agents needed to achieve blood pressure targets and adverse events. Studies with fewer than 50 participants per group or less than one year of follow-up were excluded.

Included studies compared low blood pressure targets (mean arterial pressure <92mmHg or <130/80mmHg) with usual blood pressure targets (mean arterial pressure ≤107mmHg or diastolic blood pressure <90mmHg). Participants had stage 3-4 chronic kidney disease. Cause of chronic kidney disease varied between trials. None of the trials recruited patients with diabetes. Details of antihypertensive regimens and proteinuria subgroups varied.

All authors were involved in selecting studies for the review.

**Assessment of study quality**
Quality of RCTs and follow-up reports was rated as good, fair or poor; no details of the criteria used were reported in the paper. Studies were rated by one author, confirmed by another and finalised at a meeting of all the authors. Quality of subgroup analyses by baseline proteinuria was assessed using a separate checklist (details reported in the paper).

**Data extraction**
Data were extracted by one author and checked by another.

**Methods of synthesis**
Data were summarised in tables and a narrative synthesis was presented. Differences between studies were discussed in the text.

**Results of the review**
Three RCTs (2,272 participants) were included. All were rated good quality. Observational follow-up reports (rated fair quality) were included for two of the RCTs. Mean or median follow-up ranged from 1.6 to 3.8 years. Post-trial follow-up was 6.2 to 12.2 years.

The three trials did not show benefit of the lower blood pressure target for clinical outcomes. The only statistically
significant result was in the follow-up of one trial, which showed a 23% reduction (95% confidence interval 18% to 43%) in hazard for kidney failure with the low target. The low blood pressure target groups generally required more antihypertensive medications (drugs or drug classes) and had significantly higher rates of some adverse events.

Eleven results were reported for proteinuria subgroups. Seven showed benefits for the low blood pressure target in higher proteinuria subgroups. Benefits were seen in patients with proteinuria of greater than 300mg/day in one trial and greater than 1,000mg/day in a second trial. Inconsistencies between interaction tests and subgroup analyses were seen within and between studies.

**Authors' conclusions**
Available evidence did not prove that a blood pressure target of less than 130/80mmHg improved outcomes more than a target of less than 140/90mmHg in adults with chronic kidney disease. Further research was needed to determine whether a lower target benefits patients with proteinuria above 300mg/day to 1,000mg/day.

**CRD commentary**
The review question and inclusion criteria were clear. The main search was limited to two electronic databases, so it was possible that relevant studies were missed. The authors did not search for unpublished studies, so there was a risk of publication bias. Appropriate methods were used to minimise reviewer errors and bias in study selection, validity assessment and data extraction. Criteria used for validity assessment were not reported, so the authors' assessments could not be independently verified. Relevant details of included studies were reported. A narrative synthesis was appropriate in view of the heterogeneity of the included studies. Differences between studies were investigated. Subgroup analysis was used to investigate whether patients with higher levels of proteinuria might benefit from lower blood pressure targets. This analysis was limited by reliance on aggregated rather than individual participant data and the authors' cautious interpretation was appropriate.

Despite some limitations in the review methods and reporting, the authors’ conclusions are in line with the evidence presented and seem likely to be reliable.

**Implications of the review for practice and research**
**Practice:** The authors stated that practitioners should base blood pressure targets for patients with chronic kidney disease and proteinuria on individual risk-benefit assessment and the patient's tolerance and preferences. They also stated that treatment to a lower target may require care to avoid symptoms and adverse events related to hypotension.

**Research:** The authors stated that future research should address blood pressure targets for patients with diabetes and chronic kidney disease.

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